Phytosome is a novel emerging technique in herbal drug technology and it is a patented technology developed by a leading manufacturer of drugs and nutraceuticals, to incorporate standardized plant extracts or water soluble phytoconstituents into phospholipids to produce lipid compatible molecular complexes, called as Phytosomes which improves their absorption and bioavailability. For good bioavailability, natural products must have a good balance between hydrophilicity (for dissolving into the gastrointestinal fluids) and lipophilicity (to cross lipidic bio membranes). The Phytosome process produces a little cell which protects the valuable components of the herbal extract from destruction by digestive secretions and gut bacteria and they are better able to transit from a hydrophilic environment into the lipid-friendly environment of the enterocyte cell membrane and from there into the cell and finally reaching the blood.

**Phytosome Technology:** A stoichiometric amount of phosphatidylcholine (phospholipid) is allowed to react with standard extract in a non-polar solvent. Phosphatidylcholine being a bifunctional compound possessing a lipophilic phosphatidyl moiety and hydrophilic choline moiety. The water soluble constituents like flavonoids and terpenoid of plant extracts have the affinity to bind directly with hydrophilic moiety (choline group) through chemical bonds and forms the body, while the lipid soluble phosphatidyl moiety forms tail and envelops the choline bound material. As a result, a lipid compatible molecular complex is formed called Phytosome, which helps in improvement of bioavailability of water soluble Phytoconstituents.
Molecular organization of the Phytosome (left) and Liposome (right)

The basic difference between liposomes and Phytosomes is that, Liposomes are enclosed vesicles formed by lipid materials, such as phospholipids, dispersed in an aqueous medium. One or more bilayers are formed, which have a similar structure to the cell membrane, separating the inner water phase from the outer. Whereas in Phytosomes, it is an integral part of the membrane, being the molecules stabled through chemical bonds to the polar head of the phospholipids.

Preparation of Phytosomes: Phytosomes are prepared by reacting 3-1 moles of a natural or synthetic phospholipid, such as phosphatidylcholine or phosphatidyserine etc., with one mole of component either alone or in the natural mixture in aprotic solvent such as dioxane, acetonitrile or acetone .The complex formed can be isolated by precipitation with non-solvent such as hexane, diethyl ether or by lyophilization or by spray drying. In the complex formation of Phytosomes the ratio between these two moieties generally in the range from 0.5-2.0 moles.The Phytosomes can be prepared by following methods

Solvent evaporation method

A natural or synthetic phospholipid and phytoconstituents are suspended in an appropriate solvent, and further refluxed for few hours. The resultant clear mixture is being evaporated under vacuum.

Salting out method

The Phytoconstituents or standardized extract and phospholipid is dissolved in an aprotic solvent and the solution is being stirred overnight then the formed complex is isolated from by precipitation from non-solvent like n-hexane.

Lyophilization Technique

Phospholipid and Phytoconstituents is dissolved in different solvent andfurthersolution containing Phytoconstituents were added to a solution containing phospholipid followed by stirring till complex formation takes place. The formed complex is isolated by lyophilization

Characterization of phytosomes: The factors such as the physical size, membrane permeability, percentage of entrapped solutes, and chemical composition of the preparing materials plays a vital role in determining the behavior of Phytosome in physical and biological system. The different evaluation techniques used for Phytosome drug delivery are

Percentage Yield: The Percentage yield of Phytosome can be calculated by the following formula

\[
\text{% yield}= \frac{(\text{Practical yield})}{(\text{Theoretical yield})} \times 100
\]

Visualization: The shape and size of Phytosomes can be assessed by transmission electron microscopy (TEM) or by scanning electron microscopy (SEM).

Vesicle size and Zeta Potential: The particle size and zeta potential can be measured by dynamic light scattering (DLS) by using a computerized inspection system and photon correlation spectroscopy (PCS).

Entrapment efficiency: The entrapment efficiency of herbal formulations of drug can be measured by the ultracentrifugation technique.

Transition temperature: The transition temperature of the vesicular systems can be measured by differential scanning calorimetry (DSC).

Surface tension property measurement: The surface tension property of the drug in aqueous solution can be measured by using DuNouy ring tensiometer.

Vesicle stability: The stability of vesicles can be measured by assessing the size and Structure of the vesicles over time and the mean size is measured by DLS (Dynamic Light Scattering) and structural changes are monitored by TEM (Transmission Electron Microscopy).

The spectroscopic evaluation helps us to confirm the formation of complex between Phytoconstituents and the phospholipids moiety as well as to study the corresponding interactions.

The widely employed methods are NMR and FTIR

NMR: The NMR spectra are employed for determining the complex formation between the active Phytoconstituents and the phosphatidylcholine molecule.

FTIR: The formed phytosome complex can be confirmed by FTIR simply by comparing the spectrum of the complex and the individual components and that of the mechanical mixtures. FTIR can also be considered as a valuable tool in confirming the stability of the Phytosome complex.

Properties of phytosomes

Physical properties

- Phytosome has lipophilic substances with a clear melting point.
- Average size of Phytosome ranges from 50 nm to a few hundred μm.
- They are easily soluble in non-polar solvents, insoluble in water and moderately soluble in fats.
• Liposomal like structures of miscellar shape are formed when Phytosome are treated with water

**Chemical properties**

• From spectroscopic analysis data it confirms, that there is a hydrogen bond formation between the polar head of phospholipids (i.e. phosphate and ammonium groups) and the polar functionalities of the substrate.
• From the $^1$H NMR and $^{13}$C NMR data, it can be deduced that the fatty chain gives unchanged signals both in free phospholipid and in the complex, which indicates that long aliphatic chains are wrapped around the active principle, producing lipophilic envelope.

**Biological Properties:** Herbal extracts when developed in the form of Phytosome, display better absorption, utilization and as a result produce better results than conventional herbal extracts which leads to an increase in bioavailability over the non complexed botanical derivatives.

**MERITS OF PHYTOSOMES**

• Manufacture of Phytosomes is simple
• The Phytosomes shows better stability due to Chemical bonds formed between phosphatidylcholine molecule and phytoconstituents
• The permeability of phytoconstituents can be enhanced across the biological membranes
• The absorption of lipid insoluble polar phytoconstituents can be enhanced showing improved bioavailability
• Appreciable drug entrapment can be achieved
• Phytosome process produces a little cell whereby the components of the herbal extract are protected from damage by digestive secretions and gut so that duration of action is increased
• Phosphatidylcholine used in formation of Phytosomes, besides acting as a carrier also possesses several therapeutic properties and gives the synergistic effect
• Dose requirement is also reduced

**Applications of Phytosomes**

• Phytosomes are used in the handling of liver disease include alcoholic hepatic steatosis, drug induced liver damage and hepatitis
• They are used in pharmaceutical and in beauty composition
• Phytosomes are used to treat acute and chronic liver disease of toxic metabolic or infective source or of degenerative environment
• They are used as brain stimulant, Immunomodulator, skin improver, ant wrinkle, anti-aging etc
• They are used as antioxidant, e.g. - grape seed
• They are used in hyperlipidemia, vein and skin disorder
• They are used as cancer chemo preventive agent and use to care of benign prostate hyperplasia.
• They are also used to treat hypertension

**Conclusion**

Phytosome technology can be utilized in pharmaceutical industries to solve the bioavailability and absorption related problems for various herbal formulations and provides better and effective treatment in various diseases like diabetes, hepatic toxicity and ageing etc. The recent trend is to improve the therapeutic performance of the conventional herbal drugs by formulating them as a new drug delivery system rather than going for costly research for a new entity.

**REFERENCES**